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Photocontact Allergy Test of Piroctone Olamine in the Guinea Pig

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Summary

The photocontact allergy test of piroctone olamine (PO) was carried out with guinea pigs. As the positive control substances, 3,3',4',5-tetrachlorosalicylanilide (TCSA) and 3,5,4'-tribromosalicylanilide (TBS) were used.

The animals challenged with 0.03 - 1% of PO showed no cutaneous signs, with or without UV irradiation. By contrast, the skin reactions at the UV-irradiated site of the TCSA group were severer (erythema and edema) in all the 5 animals than those at the non-irradiated site, and redness appeared only at the UV-irradiated site in 4 of the 5 animals tested with TBS.

From these results, it is not considered that PO causes photocontact sensitization.

Piroctone olamine (PO) is intended for use as an antipruritic and antidandruff agent in shampoos and rinses. The aim of this study was to assess PO for its capacity to cause photocontact allergy.

Materials and Methods

1. Animals

Male Hartley white guinea pigs obtained from Japan Laboratory Animals, Inc. were acclimated to maintenance conditions for at least one week and subjected to study. When used, the animals weighed 338 - 380 g. Throughout the acclimation and experimental periods, they were housed in individual metallic cages and given a pelleted diet (CLEA Stock Diet CR-3, CLEA Japan, Inc.) and tap water ad libitum. The animal room was maintained at 23±1°C and 55±5% of relative humidity.

2. Compounds

PO supplied by Nippon Hoechst Co., Ltd. (Lot No. H016) was used. The positive control substances used were 3,3',4',5-tetrachlorosalicylanilide (TCSA, Kanto Chemical Co., Inc.) and 3,5,4'-tribromosalicylanilide (TBS, Tokyo Kasei Kogyo Co., Ltd.).

3. Compound concentrations

As a result of the preliminary test, 5% of PO having not produced severe crust was selected as the sensitizing concentration in order to minimize effects on dermal absorption of the compound and dermal permeability to the UV light. The highest challenge concentration of PO was 1% which had been found to be the maximal non-irritant concentration and to be a non-phototoxic one in our previous studies [1,2]. The lower concentrations selected were 0.3, 0.1, and 0.03%. The sensitizing and challenge concentrations of either positive control substance were 2 and 1%, respectively; these were preliminarily shown to be positive for photocontact allergy.

PO was dissolved in propylene glycol because of its low solubility in water. As the vehicle of TCSA and TBS, acetone was selected according to the method of Morikawa [3].

4. Source of light

Two types of UV lamp were used. One was a lamp capable of emitting light at 280 - 370 nm (max. 305 nm) (FL20S·E-30, Toshiba Medical Supply), and the other, a lamp with the irradiation capacity at 300 - 430 nm (max. 352 nm) (FL20S·BLB, Toshiba); these were hereafter referred to as "SE lamp" and "BLB lamp", respectively.

5. Procedure

Ten guinea pigs were used to test PO, and 5 animals each, to test TCSA and TBS. The test was done by the method of Morikawa [3] as follows.

Sensitization was made by topical application with 0.05 ml of test compound solution to a 2 x 2 cm area on the skin over the scapula previously shaved plus UV irradiation of the same area at 1.2×10^8 ergs/cm^2 with 3 SE lamps and 3 BLB lamps (arranged alternately) for 2 hr starting 30 min after the topical application; this set of treatment was done 10 times over a period of 2 weeks (once a day, 5 times/week).

Challenge was done singly 2 weeks after the last sensitization. Two 1 x 2 cm areas (one on each side of the midline) on the back previously shaved were marked, and each was applied with 0.02 ml of test compound solution (in the PO group, 4 pairs of areas were prepared in each animal to apply with the 4 concentrations simultaneously). One area was covered with an aluminum sheet, and the other, uncovered. The areas were then irradiated at 1.2×10^8 ergs/cm^2 through a glass plate 5 mm thick with 4 BLB lamps for 2 hr.

The challenge sites were observed for cutaneous changes at 24, 48, and 72 hr after the end of the irradiation, and the skin at the uncovered site (UV-irradiated) was compared with the one at the covered site (non-irradiated).

Results

The test results are summarized in Table 1.

In the PO group, the challenge at 0.03 - 1% caused no cutaneous reactions at either of the covered and uncovered sites at any time point (Photos 1 - 3), showing no signs of photocontact allergy.

In the TCSA group, slight erythema was observed at the covered site in 2 of the 5 animals when examined at 24 hr. The cutaneous change at the site became severer in degree and incidence thereafter; at 72 hr, slight erythema was noted in 3 animals, moderate change in another animal, and severe one with edema in the other animal (Photo 4). The cutaneous signs at the UV-irradiated site in this group were apparently severer than those at the covered site; the findings at 24 hr were moderate erythema in one animal and severe one with edema in the other 4, and those at 48 and 72 hr included severe erythema and edema in all the animals (Photo 4).

The covered site in the TBS group showed no signs at any time point, while the irradiated site exhibited redness, though slightly, in 3 and 4 animals at 48 and 72 hr (Photo 5), respectively.

Discussion

The guinea pigs sensitized with 5% of PO and challenged with 0.03 - 1% of PO showed no cutaneous signs at the UV-irradiated or non-irradiated site.

By contrast, TCSA caused slight erythema even at the non-irradiated site and markedly severer signs (in all animals) at the irradiated site. TBS also induced redness of the skin only at the irradiated site. These results show both substances to induce photocontact sensitization.

The slight change noted at the non-irradiated site in the TCSA group may have been caused by the contact sensitizing ability that the substance was reported to have [4,5], but a possibility cannot be denied that the change might be a weak sign of photocontact allergy produced by a trace of UV light from the fluorescent lamps in the animal room, to which the animals were exposed after the end of the challenge.

From the results of this test, PO is not considered to cause photocontact sensitization.

References

1. S. Tanaka et al.: Primary irritancy study of piroctone olamine, unpublished data.

2. T. Inoue et al.: Phototoxicity study of piroctone olamine, unpublished data.

3. T. Morikawa: Local irritancy tests. In: "Environmental Toxicology: Method and Safety Evaluation" (ed. Y. Shirasu and O. Matsuoka), p. 458, Soft Science, Inc., Tokyo (1975).

4. T. Morikawa: Metabolism of hapten, Rinsho Hifuka (Journal of clinical dermatology) 25, 273-285 (1971).

5. T. Horio: Study on photocontact allergy of halogenated salicylanilides, Hifuka Kiyo (Journal of dermatology) 71, 2-25 (1976).

This investigation was carried out from November, 1982, to March, 1983.

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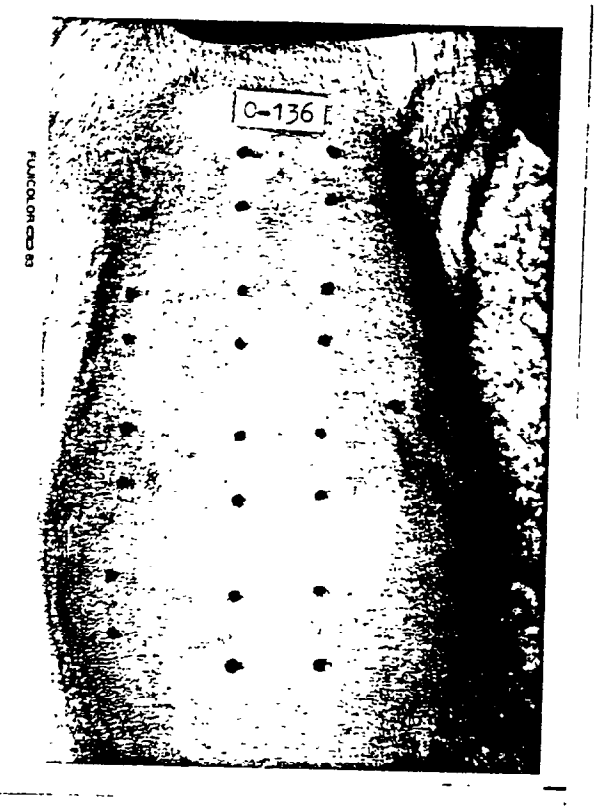
Table 1 Photocontact allergy test of piroctone olamine in guinea pigs

Compound	Sensitizing concentration (%)	Challenge		No. of animals	Time after challenge (hr)											
		Concentration (%)	UV*		24				48				72			
					No. of animals with changes rated**											
					0	1	2	3	0	1	2	3	0	1	2	3
Piroctone olamine	5.00	0.03	+	10	10	0	0	0	10	0	0	0	10	0	0	0
			-	10	10	0	0	0	10	0	0	0	10	0	0	0
		0.10	+	10	10	0	0	0	10	0	0	0	10	0	0	0
			-	10	10	0	0	0	10	0	0	0	10	0	0	0
		0.30	+	10	10	0	0	0	10	0	0	0	10	0	0	0
			-	10	10	0	0	0	10	0	0	0	10	0	0	0
		1.00	+	10	10	0	0	0	10	0	0	0	10	0	0	0
			-	10	10	0	0	0	10	0	0	0	10	0	0	0
TCSA	2.00	1.00	+	5	0	0	1	4	0	0	0	5	0	0	0	5
			-	5	3	2	0	0	1	2	1	1	0	3	1	1
TBS	2.00	1.00	+	5	5	0	0	0	2	3	0	0	1	4	0	0
			-	5	5	0	0	0	5	0	0	0	5	0	0	0

* +: The site was irradiated with UV.
-: The site was protected from UV with an aluminum sheet.

** The ratings are: 0, no visible change; 1, slight or discrete erythema; 2, moderate erythema; 3, severe erythema and edema.



Left	Right
Irradiated with UV	Protected from UV

Photo 1 Back skin of a guinea pig observed 24 hr after challenge

Sensitization: 5% piroctone olamine (PO)
Challenge: 0.03 - 1.0% PO

Each square (2 x 1 cm) inside the 4 solid circles is the application site.

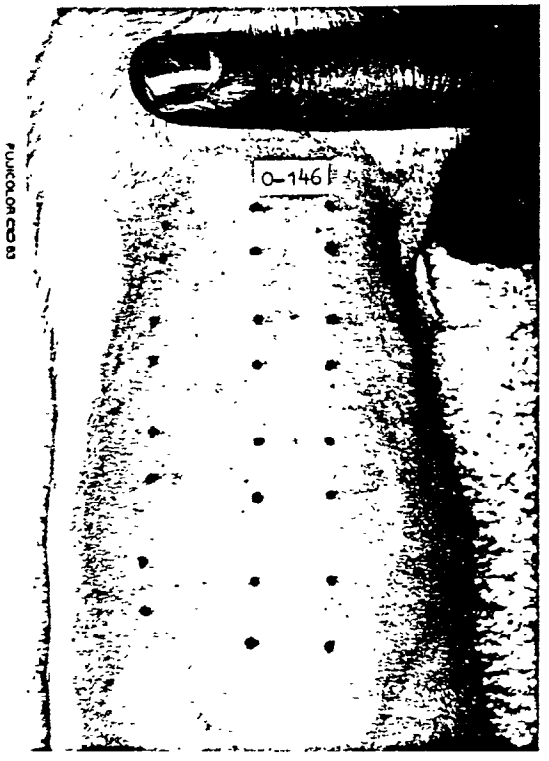


Photo 2 Back skin of a guinea pig observed 48 hr after challenge

Sensitization: 5% piroctone olamine (PO)
Challenge: 0.03 - 1.0% PO

Each square (2 x 1 cm) inside the 4 solid circles is the application site.

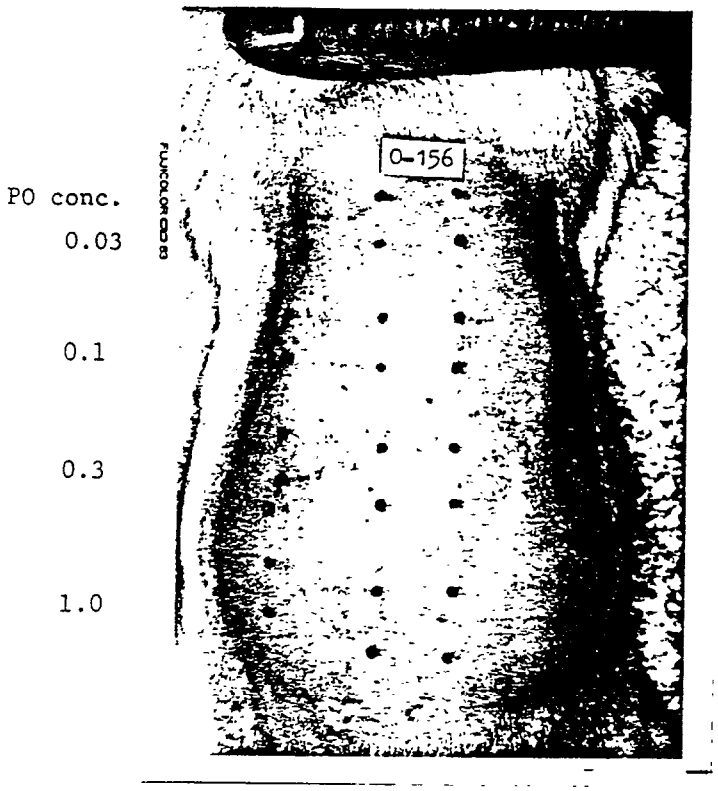
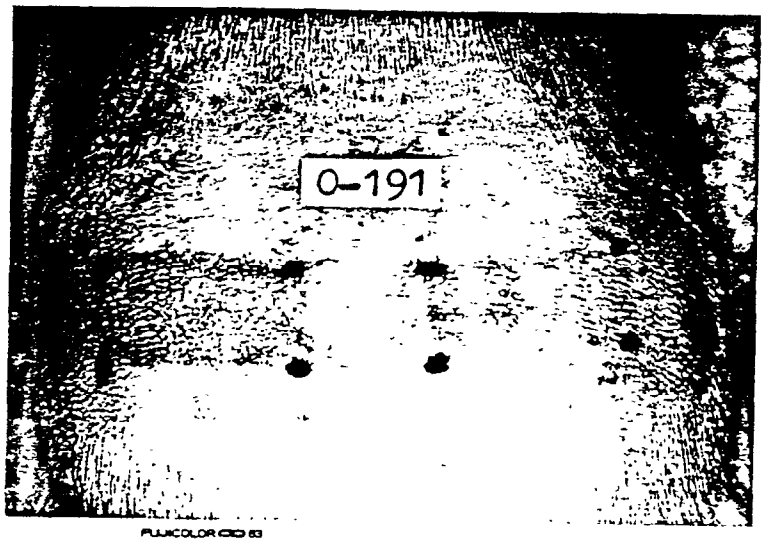


Photo 3 Back skin of a guinea pig observed 72 hr after challenge

Sensitization: 5% piroctone olamine (PO)
Challenge: 0.03 - 1.0% PO

Each square (2 x 1 cm) inside the 4 solid circles is the application site.

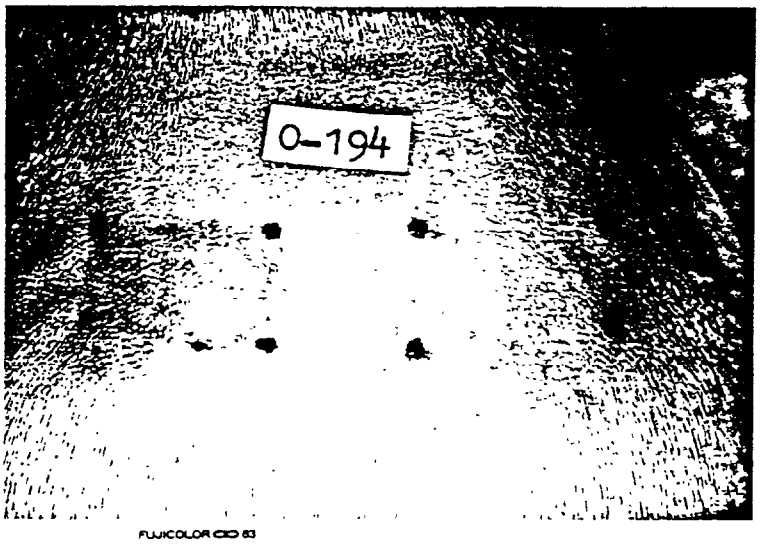


Left	Right
Irradiated with UV	Protected from UV

Photo 4 Back skin of a guinea pig observed 72 hr after challenge

Sensitization: 2% TCSA
Challenge: 1% TCSA

Each square (2 x 1 cm) inside the 4 solid circles is the application site.



Left	Right
Irradiated with UV	Protected from UV

Photo 5 Back skin of a guinea pig observed 72 hr after challenge

Sensitization: 2% TBS
Challenge: 1% TBS

Each square (2 x 1 cm) inside the 4 solid circles is the application site.